



Early Adoption and Diffusion of Oral Semaglutide in US Adults With Obesity

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Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have expanded the pharmacologic treatment options for obesity.¹ Although these therapies were previously available only as injectables, oral semaglutide, the first oral GLP-1 RA (approved for type 2 diabetes [T2D] in 2019, and for obesity in December 22, 2025),² may improve treatment accessibility and patient acceptance.³ However, general population evidence on early adoption of oral semaglutide for obesity after market introduction remains limited. This study evaluated early treatment trends of oral semaglutide among adults eligible for obesity management medications (OMMs) following its approval for obesity.

+ Supplemental content

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Methods

This retrospective cohort study followed the [STROBE](#) reporting guidelines and used deidentified electronic health record (EHR) data from Epic Cosmos, which includes more than 300 million patient records from over 2000 hospitals and 47 100 clinics across the US. This study was exempt from institutional review board review, and informed consent was waived because only deidentified data were used, in accordance with 45 CFR §46. We defined patients eligible for OMM as adults aged 18 years or older with a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) greater than or equal to 30, or greater than or equal to 27 with at least 1 obesity-related comorbidity (eg, hypertension, dyslipidemia, obstructive sleep apnea, atherosclerotic cardiovascular disease, and heart failure) (eTable 1 in [Supplement 1](#)).⁴ Patients without a recorded BMI or with T2D were excluded, to focus on obesity management.⁵ Detailed methods are provided in eMethods in [Supplement 1](#).

Within the eligible cohort, new initiators of oral semaglutide, injectable semaglutide, and injectable tirzepatide were identified between December 22, 2025, and March 15, 2026. New initiation was defined as a first prescription for the study drug with no prescription for the same drug during the preceding 12 months (eTable 2 in [Supplement 1](#)). The index date was the date of the first recorded prescription in the EHR. Race and ethnicity were obtained from structured demographic fields in the EHRs of participating health care organizations and harmonized within Epic Cosmos and are included in this study to characterize the demographic composition of the study population and potential differences in obesity medication use.

The primary outcome was the weekly incidence of oral semaglutide initiation, calculated as the number of new initiators per 10 000 OMM-eligible adults per week, to capture new uptake and minimize the influence of prevalent users. Weekly incidence rates were also estimated for injectable semaglutide and tirzepatide for comparison. To evaluate uptake among GLP-1 RA-naïve patients, we repeated the analyses after excluding individuals with any prior GLP-1 RA use.

Among oral semaglutide initiators, prior GLP-1 RA use during the preceding 12 months was assessed to distinguish treatment substitution or expansion. Because the analyses were descriptive, no hypothesis testing was performed. Analyses were conducted using R statistical software version 4.5.1 (R Project for Statistical Computing).

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Table. Baseline Characteristics of GLP-1 RA Initiators Among Adults Eligible for Obesity Medication Management Without Type 2 Diabetes, December 22, 2025, to March 15, 2026

Variable	Patients, No. (%)				SMD ^a	
	Eligible cohort (N = 47 894 786)	Oral semaglutide (n = 148 792)	Injectable semaglutide (n = 227 040)	Injectable tirzepatide (n = 355 513)	Oral vs injectable semaglutide	Oral semaglutide vs injectable tirzepatide
Age at index, mean (SD), y	52.4 (17.7)	53.3 (14.4)	49.7 (14.3)	50.5 (14.1)	0.255 ^b	0.199 ^b
Sex						
Female	27 617 003 (57.7)	108 162 (72.7)	159 038 (70.0)	238 434 (67.1)	0.059	0.123 ^b
Male	20 264 393 (42.3)	40 609 (27.3)	67 959 (29.9)	117 010 (32.9)		
Other	13 390 (<0.1)	21 (<0.1)	43 (<0.1)	69 (<0.1)		
Race						
American Indian or Alaska Native	528 415 (1.1)	1042 (0.7)	2550 (1.1)	3305 (0.9)	0.121 ^b	0.056
Asian	997 127 (2.1)	2301 (1.5)	4311 (1.9)	6513 (1.8)		
Black or African American	6 744 348 (14.1)	18 671 (12.5)	34 514 (15.2)	45 750 (12.9)		
Native Hawaiian or other Pacific Islander	169 073 (0.4)	282 (0.2)	628 (0.3)	946 (0.3)		
White	28 234 125 (59.0)	100 854 (67.8)	143 555 (63.2)	234 964 (66.1)		
Other ^c	11 221 698 (23.4)	25 642 (17.2)	41 482 (18.3)	64 035 (18.0)		
Ethnicity						
Hispanic or Latino	4 971 560 (10.4)	8392 (5.6)	18 628 (8.2)	26 751 (7.5)	0.104 ^b	0.080
Not Hispanic or Latino	32 387 943 (67.6)	114 079 (76.7)	167 203 (73.6)	263 861 (74.2)		
Other ^d	10 535 283 (22.0)	26 321 (17.7)	41 209 (18.2)	64 901 (18.3)		
Baseline body mass index ^e						
Mean (SD)	33.7 (6.2)	36.6 (7.2)	37.6 (7.5)	38.0 (7.6)	0.131 ^b	0.190 ^b
Median (IQR)	32.3 (29.6-36.5)	35.2 (31.4-40.3)	36.2 (32.2-41.4)	36.6 (32.5-42.0)		
Urbanicity (Rural-Urban Commuting Area)						
Metropolitan	39 810 679 (83.1)	127 596 (85.8)	193 916 (85.4)	306 434 (86.2)	0.030	0.020
Micropolitan	4 020 146 (8.4)	11 455 (7.7)	17 587 (7.7)	25 870 (7.3)		
Small town	1 903 799 (4.0)	4863 (3.3)	7322 (3.2)	11 112 (3.1)		
Rural	1 311 957 (2.7)	3289 (2.2)	5049 (2.2)	7948 (2.2)		
Other or unknown	848 205 (1.8)	1589 (1.1)	3166 (1.4)	4149 (1.2)		
Comorbidities						
Hypertension	19 147 215 (40.0)	69 104 (46.4)	98 180 (43.2)	154 264 (43.4)	0.064	0.061
Dyslipidemia	19 069 828 (39.8)	74 058 (49.8)	104 676 (46.1)	162 934 (45.8)	0.073	0.079
Obstructive sleep apnea	5 321 752 (11.1)	28 069 (18.9)	46 646 (20.5)	116 684 (32.8)	0.042	0.323
Atherosclerotic cardiovascular disease	7 192 972 (15.0)	15 903 (10.7)	26 741 (11.8)	34 868 (9.8)	0.035	0.029
Heart failure	2 164 703 (4.5)	3862 (2.6)	7992 (3.5)	10 722 (3.0)	0.054	0.025
Insurance ^f						
Miscellaneous or other	35 036 065 (73.2)	122 715 (82.5)	192 216 (84.7)	301 054 (84.7)	0.163 ^b	0.124 ^b
Medicare	7 093 143 (14.8)	19 972 (13.4)	21 047 (9.3)	36 198 (10.2)		
Medicaid	3 381 136 (7.1)	4643 (3.1)	11 750 (5.2)	15 793 (4.4)		
Self-pay	2 007 575 (4.2)	1168 (0.8)	1468 (0.6)	1813 (0.5)		
Unknown	376 867 (0.8)	294 (0.2)	559 (0.2)	655 (0.2)		
Prescriber specialty						
Family medicine	NA	76 577 (51.5)	112 864 (49.7)	175 746 (49.4)	0.155 ^b	0.193 ^b
Internal medicine	NA	29 874 (20.1)	41 677 (18.4)	68 439 (19.3)		
Primary care	NA	18 451 (12.4)	27 140 (12.0)	43 724 (12.3)		
Bariatrics	NA	6784 (4.6)	11 582 (5.1)	15 625 (4.4)		
Endocrinology	NA	5691 (3.8)	9557 (4.2)	15 353 (4.3)		
Cardiology	NA	2698 (1.8)	7137 (3.1)	8392 (2.4)		
Others	NA	8717 (5.9)	17 083 (7.5)	28 234 (7.9)		

(continued)

Table. Baseline Characteristics of GLP-1 RA Initiators Among Adults Eligible for Obesity Medication Management Without Type 2 Diabetes, December 22, 2025, to March 15, 2026 (continued)

Variable	Patients, No. (%)				SMD ^a	
	Eligible cohort (N = 47 894 786)	Oral semaglutide (n = 148 792)	Injectable semaglutide (n = 227 040)	Injectable tirzepatide (n = 355 513)	Oral vs injectable semaglutide	Oral semaglutide vs injectable tirzepatide
Prior GLP-1 RA (12 mo)						
Any prior GLP-1 RA	NA	69 931 (47.0)	NA	NA		
Injectable semaglutide	NA	42 994 (28.9)	NA	NA		
Injectable tirzepatide	NA	40 868 (27.5)	NA	NA		
Liraglutide	NA	1901 (1.3)	NA	NA	NA	NA
Dulaglutide	NA	439 (0.3)	NA	NA		
Other GLP-1 RA	NA	18 (<0.1)	NA	NA		
No prior GLP-1 RA	NA	78 861 (53.0)	NA	NA		
Oral semaglutide product						
Oral Wegovy	NA	130 312 (87.6)	NA	NA		
Rybelsus	NA	18 480 (12.4)	NA	NA	NA	NA

Abbreviations: GLP-1 RA, glucagon-like peptide-1 receptor agonist; NA, not applicable; SMD, standardized mean difference.

^a Pairwise SMDs compare oral semaglutide with each injectable group. For continuous variables, SMD was calculated as the difference in means divided by the pooled SD. For categorical variables, the maximum SMD across individual categories is reported.

^b Denotes SMD greater than 0.1.

^c The other category included patients recorded as other race or whose race was unknown.

^d The other category included patients recorded as whose ethnicity was unknown.

^e Body mass index is calculated as weight in kilograms divided by height in meters squared.

^f Insurance reflects the insurance information recorded in the Epic Cosmos rather than actual payment to obtain the prescription; the miscellaneous or other category is primarily aligned with commercial insurance.

Results

Among 47 894 786 OMM-eligible individuals (mean [SD] age, 52.4 [17.7] years; 27 617 003 female [57.7%]), 148 792 initiated oral semaglutide during the study period. Of these, 130 312 (87.6%) received oral Wegovy and 18 480 (12.4%) received Rybelsus (both from Novo Nordisk). Compared with initiators of injectable semaglutide or tirzepatide, oral semaglutide initiators were generally older (mean [SD] age, 53.3 [14.4] years) and more likely to be female (108 162 patients [72.7%]), with lower baseline BMI (mean [SD], 36.6 [7.2]) and higher coverage by Medicare (19 972 individuals [13.4%]) (Table).

Following Food and Drug Administration approval, weekly oral semaglutide initiation increased rapidly from nearly 0 to a peak of 4.56 per 10 000 OMM-eligible adults (95% CI, 4.50-4.62 per 10 000 OMM-eligible adults) in week 10, March 2 to 8 (Figure). Oral semaglutide's uptake quickly approached that of injectable semaglutide and briefly exceeded it, whereas tirzepatide consistently had the highest weekly initiation rate throughout the period. Among GLP-1 RA-naïve adults, temporal trends were similar, although oral semaglutide initiation remained below that of injectable semaglutide. Overall, 53.0% of oral semaglutide initiators (78 861 individuals) had no prior GLP-1 RA use, while prior exposure was most common among those using injectable semaglutide (42 994 individuals [28.9%]) or injectable tirzepatide (40 868 individuals [27.5%]) (Table).

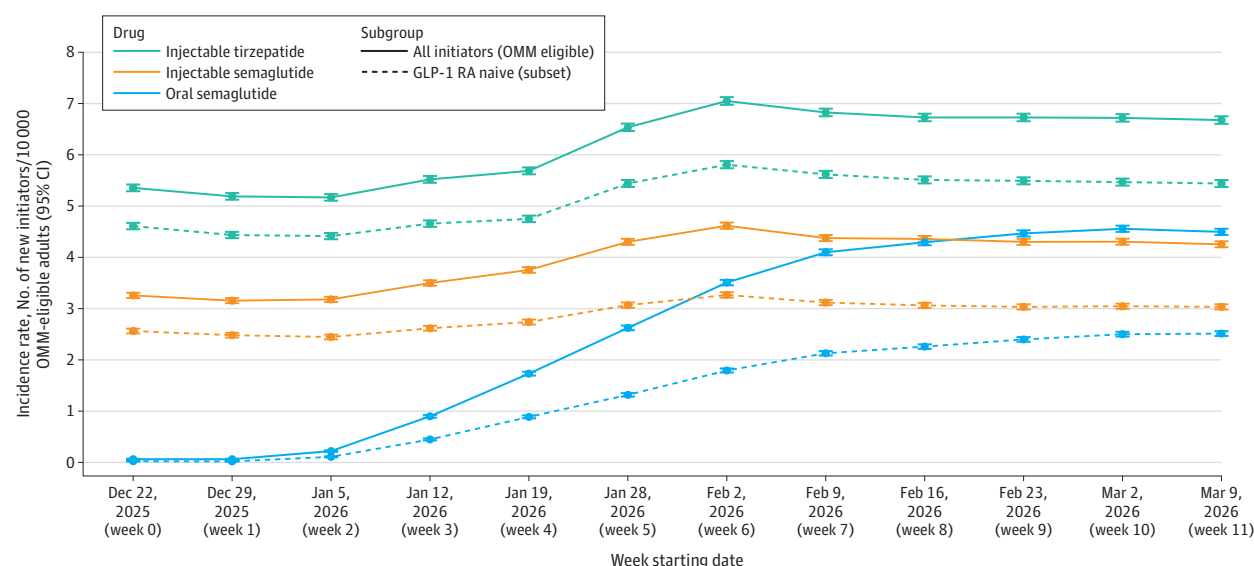
Discussion

In this national cohort of over 47 million adults eligible for OMMs, oral semaglutide was rapidly adopted following its Food and Drug Administration approval for obesity, with weekly initiation rates approaching those of injectable semaglutide within 3 months. More than half of oral semaglutide

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Figure. Line Graph of Weekly Incidence of Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA) Initiation Among Adults Meeting Obesity Medication Management (OMM) Criteria Without Type 2 Diabetes



Graph shows weekly incidence of new initiation per 10 000 eligible adults from December 22, 2025 (Food and Drug Administration approval of oral semaglutide for weight management) through March 15, 2026 (week of March 9); the x-axis indicates the first day of each week. Solid lines denote the full eligible cohort (N = 47 894 786);

dashed lines denote the subset without GLP-1 RA dispensing in the preceding 12 months (n = 45 186 876), with rates calculated using each cohort's own denominator. New initiation required a 12-month washout of the index drug. Error bars indicate 95% CIs.

initiators had no prior GLP-1 RA use, suggesting that early uptake reflected both expansion to new users and switching from existing GLP-1 RA therapies.⁶

The availability of an oral GLP-1 RA, including oral semaglutide and the recent approval of orforglipron in April 2026,⁷ may reduce barriers associated with injectable therapies and expand access to pharmacologic obesity treatment.^{6,8} Oral semaglutide initiators were generally older, female, with lower BMI, and more likely to have Medicare coverage. However, tirzepatide remained the most frequently initiated obesity medication during the study period, potentially reflecting its greater weight-loss efficacy and established clinical use.

This study has several limitations. First, prescribing indications were not available in the EHR, although exclusion of adults with T2D reduced potential indication misclassification. Second, prescription orders may not reflect medication dispensing or use, and prescriptions outside participating Epic health systems (eg, online and direct-to-consumer platforms) may not have been captured. Third, delays in data availability may have limited ascertainment of early uptake. Fourth, this descriptive study was not designed to assess causal effects, and potential confounding or other biases were not adjusted for. Future longer-term studies are needed to evaluate persistence, adherence, and clinical outcomes associated with oral GLP-1 RA use in routine practice.

ARTICLE INFORMATION

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Author Contributions: Ms Lei and Dr Chen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Ms Lei and Dr Tang are co-first authors. Drs Asch and Chen are senior authors.

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Data Sharing Statement: See [Supplement 2](#).

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SUPPLEMENT 1.

eMethods. Data Source, Eligibility for Obesity Management Medications, Exposure Definitions, and Incidence Rate Calculation

eTable 1. *ICD-10-CM* Codes Defining Obesity-Related Comorbidities for Eligibility
eTable 2. Medication Identification Criteria

SUPPLEMENT 2.
Data Sharing Statement